Clinical trial results:
An Open-Label Extension Study of Reslizumab 110-mg Fixed, Subcutaneous Dosing in Patients 12 Years of Age and Older with Severe Eosinophilic Asthma

Summary

EudraCT number	2016-004661-23
Trial protocol	BE HU CZ DE FR ES PL RO
Global end of trial date	22 February 2018

Results information

Result version number	v1 (current)
This version publication date	06 January 2019
First version publication date	06 January 2019

Trial information

Trial identification

Sponsor protocol code	C38072-AS-30066

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03052725
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Teva Branded Pharmaceutical Products, R&D Inc.
Sponsor organisation address	41 Moores Road, Frazer, PA, United States, 19355
Public contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 888-483-8279, info.era-clinical@teva.de
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 888-483-8279, info.era-clinical@teva.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to support the long-term safety of reslizumab 110 mg administered sc once every 4 weeks in patients 12 years of age and older with severe eosinophilic asthma that was inadequately controlled on standard-of-care treatment.

Protection of trial subjects:

This study was conducted in full accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (eg, Code of Federal Regulations [CFR] Title 21, Parts 11, 50, 54, 56, 312, and 314; European Union Directive 2001/20/EC on the approximation of the laws, regulations, and administrative provisions of the Member States relating to the implementation of GCP in the conduct of clinical trials on medicinal products for human use). The principal investigator at each study center was responsible for the conduct and administration of the study at that center and for contacts with study center management, with the IEC/IRB, and with local authorities. Written and/or oral information about the study was provided to all patients in nontechnical language understandable by the patients. The information included an adequate explanation of the aims, methods, anticipated benefits, potential hazards, and insurance arrangements in force. Written informed consent was obtained from each patient before any study procedures or assessments were done. It was explained to the patients that they were free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment. For patients aged 12 to <18 years, a signed and dated informed consent form was obtained from a parent/legally acceptable representative, and a signed and dated assent form was obtained from each patient before any study-specific procedures or assessments were done and after the aims, methods, anticipated benefits, and potential hazards were explained, according to local IRB/IEC requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Czech Republic: 17
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Hungary: 26
Country: Number of subjects enrolled	Israel: 36
Country: Number of subjects enrolled	Poland: 19

Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Russian Federation: 33
Country: Number of subjects enrolled	Ukraine: 104
Country: Number of subjects enrolled	United States: 84
Worldwide total number of subjects	391
EEA total number of subjects	130

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	17
Adults (18-64 years)	296
From 65 to 84 years	78
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 392 patients with severe eosinophilic asthma rolled over from Study 30025 or 30027, and 391 of these patients (at 125 centers) were enrolled into this extension study and treated with reslizumab. One patient withdrew consent after completing Study 30025 and before enrolling in Study 30066.

Pre-assignment

Screening details:

Of the 391 patients enrolled, 112 (29%) enrolled seamlessly and 279 (71%) enrolled non-seamlessly, meaning there was a time gap between completion of the parent study and start of this extension study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Reslizumab 110 mg; Previous Treatment Placebo

Arm description:

Participants who were administered placebo in the parent study, were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.

Arm type	Experimental
Investigational medicinal product name	Reslizumab
Investigational medicinal product code	
Other name	CINQAIR®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Reslizumab was administered as 110 mg subcutaneous (sc) injections in the thigh, abdomen, or upper arm(s) once every 4 weeks for a total of 9 doses.

Arm title	Reslizumab 110 mg: Previous Treatment Reslizumab

Arm description:

Participants who were administered reslizumab in the parent study, were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.

Arm type	Experimental
Investigational medicinal product name	Reslizumab
Investigational medicinal product code	
Other name	CINQAIR®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Reslizumab was administered as 110 mg subcutaneous (sc) injections in the thigh, abdomen, or upper arm(s) once every 4 weeks for a total of 9 doses.

Number of subjects in period 1	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab
Started	194	197
Safety Analysis Set	194	196
Completed	46	47
Not completed	148	150
Consent withdrawn by subject	3	4
Adverse event, non-fatal	2	-
Pregnancy	-	1
Study terminated by sponsor	143	144
Site closure	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Reslizumab 110 mg; Previous Treatment Placebo
Reporting group description:	
Participants who were administered placebo in the parent study, were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.	
Reporting group title	Reslizumab 110 mg: Previous Treatment Reslizumab
Reporting group description:	
Participants who were administered reslizumab in the parent study, were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.	

Reporting group values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab	Total
Number of subjects	194	197	391
Age, Customized Units: Subjects			
12 to <18 years	9	8	17
18 to <65 years	156	141	297
>=65 years	29	48	77
Age Continuous Units: years			
arithmetic mean	50.4	52.5	
standard deviation	± 14.85	± 15.62	-
Sex: Female, Male Units: Subjects			
Female	112	122	234
Male	82	75	157
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	182	185	367
Black	7	10	17
Asian	3	2	5
Other	2	0	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	18	8	26
Not Hispanic or Latino	174	187	361
Unknown or Not Reported	2	2	4
Region Group Units: Subjects			
U.S./Canada	47	41	88
Europe	131	136	267
Other	16	20	36
Weight Units: kg			
arithmetic mean	79.78	81.22	
standard deviation	± 17.647	± 18.712	-

Body Mass Index (BMI) Units: kg/m^2 arithmetic mean standard deviation	 28.377 ± 5.8288	 28.880 ± 5.9672	 -
Systemic Corticosteroid (OCS) Use at Baseline			
Daily OCS dose is defined as total OCS dose in a day (accounting for reported dose and dose frequency) and converting the total daily dose to a prednisone-equivalent dose.			
Units: mg prednisolone or equivalent arithmetic mean standard deviation	 12.01 ± 10.870	 12.26 ± 10.760	 -

End points

End points reporting groups

Reporting group title	Reslizumab 110 mg; Previous Treatment Placebo
Reporting group description:	
Participants who were administered placebo in the parent study, were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.	
Reporting group title	Reslizumab 110 mg: Previous Treatment Reslizumab
Reporting group description:	
Participants who were administered reslizumab in the parent study, were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.	

Primary: Participants With Treatment-Emergent Adverse Events (TEAEs)

End point title	Participants With Treatment-Emergent Adverse Events

End point description:

An adverse event is any untoward medical occurrence, regardless of whether it has a causal relationship with study treatment. In this study, asthma exacerbations should not be recorded as adverse events unless assessed by the investigator as more severe than the patient's usual disease course. The period for reporting treatment-emergent adverse events was defined as the period after the first dose of study drug was administered until the end of treatment visit. Relation of AE to treatment was determined by the investigator. Serious AEs include death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, OR an important medical event that jeopardized the patient and required medical intervention to prevent the previously listed serious outcomes.

End point type	Primary

End point timeframe:

Day 1 to up to Day 269; for participants who discontinued early for reasons other than study termination, the timeframe was first dose of study drug to 4 weeks after the last dose of study drug.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No intention to make inference based on stat analysis; the intent is to support clinical judgment.

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: participants				
>=1 TEAE	102	114		
>=1 treatment-related TEAE	7	6		
>=1 serious TEAE	5	11		
>=1 treatment-related, serious TEAE	0	0		
>=1 TEAE leading to discontinuation	2	0		
>=1 TEAE leading to death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With Potentially Clinically Significant Abnormal Hematology Values

End point title	Participants With Potentially Clinically Significant Abnormal Hematology Values

End point description:

Participants are included in the counts if the worst study value reaches the following clinically significant levels: Eosinophils (high): >=1.5*10^9/L and increase >0 Hematocrit (low): >=18 years old: <0.32 L/L for females; <0.37 L/L for males plus a decrease >0 for both or 12 to <18 years old: <0.30 L/L and a decrease >0 for both females and males Hemoglobin (low): >=18 years old: <=95 g/L and decrease >0; 12 to <18 years old: <=100 g/L and decrease >0 Leukocytes (high): >=20*10^9/L and increase >0 Leukocytes (low): <=3*10^9/L and decrease >0 Neutrophils (low): <=1*10^9/L and decrease >0 Platelets (low): <=75*10^9/L and decrease >0

End point type	Secondary

End point timeframe:

Week 0 (baseline), Weeks 8, 24, 36 plus any unscheduled visits

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	192		
Units: participants				
Participants with >=1 abnormality	8	5		
Eosinophils (high)	1	0		
Hematocrit (low)	4	2		
Hemoglobin (low)	2	0		
Leukocytes (high)	0	1		
Leukocytes (low)	2	0		
Neutrophils (low)	1	1		
Platelets	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With Potentially Clinically Significant Abnormal Serum Chemistry Values

End point title	Participants With Potentially Clinically Significant Abnormal Serum Chemistry Values

End point description:

Participants are included in the counts if the worst study value reaches the following clinically significant levels: Alanine Aminotransferase (high): >=3* upper limit of normal (ULN) and increase >0 Aspartate Aminotransferase (high): >=3* upper limit of normal (ULN) and increase >0 Bilirubin (high): >=34.2 micromol/L and increase >0 Blood Urea Nitrogen (high): >=10.71 mmol/L and increase >0 Creatine Phosphokinase (high): >10* ULN and increase >0 Creatine Phosphokinase (medium high): >=3.1*ULN and <=10*ULN and increase >0 Creatinine (high): >=177 micromol/L and increase >0

End point type	Secondary

End point timeframe:

Week 0 (baseline), Weeks 4, 8, 24, 36 plus any unscheduled visits

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	192		
Units: participants				
Participants with >=1 abnormality	12	10		
Alanine Aminotransferase (high)	1	2		
Aspartate Aminotransferase (high)	1	1		
Bilirubin (high)	2	1		
Blood Urea Nitrogen (high)	2	4		
Creatine Phosphokinase (high)	2	1		
Creatine Phosphokinase (medium high)	6	4		
Creatinine (high)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants' Tolerability and Injection Site Reactions by Domain and Worst Overall Severity

End point title	Participants' Tolerability and Injection Site Reactions by Domain and Worst Overall Severity

End point description:

The worst finding for participants in each tolerability and injection site domain from all treatment weeks is summarized. Local tolerability at the injection site was assessed approximately 1 hour after study drug administration. Severity was rated on a 4-level scale of none, mild, moderate and severe.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 28, and 36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: participants				
Pain - None	191	194		
Pain - Mild	3	2		
Pain - Moderate	0	0		

Pain - Severe	0	0		
Tenderness - None	193	192		
Tenderness - Mild	1	4		
Tenderness - Moderate	0	0		
Tenderness - Severe	0	0		
Erythema - None	191	188		
Erythema - Mild	2	7		
Erythema - Moderate	1	1		
Erythema - Severe	0	0		
Warmth - None	192	192		
Warmth - Mild	1	4		
Warmth - Moderate	1	0		
Warmth - Severe	0	0		
Swelling - None	191	190		
Swelling - Mild	2	5		
Swelling - Moderate	1	1		
Swelling - Severe	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Potentially Clinically Significant Abnormal Vital Sign Values

End point title	Participants with Potentially Clinically Significant Abnormal Vital Sign Values

End point description:

Participants are included in the counts if the worst study value reaches the following clinically significant levels: Diastolic blood pressure (high): >100 mmHg and increase >=12 for participants >=18 years; >85 mmHg and increase >=12 for participants 12 - < 18 years Pulse rate (high): >100 beats/minute and increase >=12 Respiratory rate (high): >24 breaths/minute and increase >=10 for participants >=18 years >20 breaths/minute and increase >=10 for participants 12 - < 18 years Systolic blood pressure (high): >160 mmHg and increase >=30 for participants >=18 years; >130 mmHg and increase >=30 for participants 12 - < 18 years Temperature (high): >38.1 celsius and increase >=1.1 Temperature (low): <35.8 celsius

End point type	Secondary

End point timeframe:

Week 0 (baseline), Weeks 4, 8, 12, 16,20, 24, 28, 32, 36 plus any unscheduled visits

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	196		
Units: participants				
Participants with >=1 abnormality	20	16		
Diastolic Blood Pressure - High	0	1		
Pulse Rate - High	1	2		

Respiratory Rate - High	2	0		
Systolic Blood Pressure - High	2	0		
Temperature - High	1	0		
Temperature - Low	14	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Clinical Asthma Exacerbations (CAEs)

End point title	Annualized Rate of Clinical Asthma Exacerbations (CAEs)

End point description:

Data is included between the first dose of study drug to the end of treatment visit for completed participants, and the first dose of study drug to 4 weeks after the last dose of study drug for patients who discontinued treatment early. Annual rate is defined as the number of events/(duration of treatment [days]/365.25). Participants with zero events are included.

End point type	Secondary

End point timeframe:

Day 1 to up to Day 269; for participants who discontinued early for reasons other than study termination, the timeframe was first dose of study drug to 4 weeks after the last dose of study drug.

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: CAEs / year				
arithmetic mean (standard deviation)	0.42 (± 1.104)	0.70 (± 1.538)		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Clinical Asthma Exacerbations (CAEs) Requiring Asthma-Specific Hospital Admissions or Emergency Room Visits

End point title	Annualized Rate of Clinical Asthma Exacerbations (CAEs) Requiring Asthma-Specific Hospital Admissions or Emergency Room Visits

End point description:

Data is included between the first dose of study drug to the end of treatment visit for completed participants, and the first dose of study drug to 4 weeks after the last dose of study drug for patients who discontinued treatment early. Annual rate is defined as the number of events/(duration of treatment [days]/365.25). Participants with zero events are included.

End point type	Secondary

End point timeframe:

Day 1 to up to Day 269; for participants who discontinued early for reasons other than study

termination, the timeframe was first dose of study drug to 4 weeks after the last dose of study drug.

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: CAEs / year				
arithmetic mean (standard deviation)	0.06 (± 0.362)	0.11 (± 0.514)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of Days of Hospital Stay During the Treatment Period

End point title	Mean Number of Days of Hospital Stay During the Treatment Period

End point description:

Participants with no hospitalizations are included.

End point type	Secondary

End point timeframe:

Day 1 to up to Day 269; for participants who discontinued early for reasons other than study termination, the timeframe was first dose of study drug to 4 weeks after the last dose of study drug

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: days				
arithmetic mean (standard deviation)	0.25 (± 1.658)	1.02 (± 7.848)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of School/Work Days Missed Due to Asthma During the Treatment Period

End point title	Mean Number of School/Work Days Missed Due to Asthma During the Treatment Period

End point description:

Participants with no school or work days missed due to asthma are included in the counts.

End point type	Secondary

End point timeframe:

Day 1 to up to Day 269; for participants who discontinued early for reasons other than study termination, the timeframe was first dose of study drug to 4 weeks after the last dose of study drug

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: days				
arithmetic mean (standard deviation)	0.11 (± 1.202)	0.00 (± 0.000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-bronchodilator Forced Expiratory Volume in One Second (FEV1): Baseline Values and Change from Baseline Values at Weeks 8, 24 and 36

End point title	Pre-bronchodilator Forced Expiratory Volume in One Second (FEV1): Baseline Values and Change from Baseline Values at Weeks 8, 24 and 36

End point description:

The FEV1 is the volume of air that can be forcibly exhaled from the lungs in the first second, measured in liters. Pre-bronchodilator spirometry assessments at designated clinic visits (weeks 0, 8, and 24, and 36) should only be performed after withholding short-acting bronchodilators (ie, inhaled short-acting beta-adrenergic agonists and/or short-acting anticholinergics) for at least 6 hours and long-acting bronchodilators ie, inhaled long-acting beta-adrenergic agonists and long acting anticholinergic agents) for at least 12 or 24 hours, according to their labeled dose schedule.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Weeks 8, 24, 36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: liters				
arithmetic mean (standard deviation)				
Baseline - observed value (n=179, 177)	2.162 (± 0.980)	2.117 (± 0.927)		

Change at Week 8 (n=175, 168)	0.099 (± 0.704)	0.031 (± 0.529)		
Change at Week 24 (n=99, 91)	0.169 (± 0.851)	-0.020 (± 0.472)		
Change at Week 36 (n=32, 31)	0.245 (± 0.677)	0.010 (± 0.550)		

Statistical analyses

No statistical analyses for this end point

Secondary: Morning Ambulatory Forced Expiratory Volume in One Second (FEV1): Baseline Values and Change from Baseline Values at Weeks 1, 4, 8, 24 and 36

End point title	Morning Ambulatory Forced Expiratory Volume in One Second (FEV1): Baseline Values and Change from Baseline Values at Weeks 1, 4, 8, 24 and 36

End point description:

A weekly average of daily morning ambulatory FEV1 (measured by the handheld spirometry device) was derived using 7-day window intervals. The average was calculated as the sum of all values divided by the number of non-missing assessments. There will be no imputation of missing data. At least 4 of the 7 measurements need to be recorded for a week to be included in the analysis; otherwise the week was treated as missing.

End point type	Secondary

End point timeframe:

Week 0 (baseline), Weeks 1, 4, 8, 24, 36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: liters				
arithmetic mean (standard deviation)				
Baseline - observed value (n=192, 193)	2.057 (± 0.814)	2.027 (± 0.848)		
Change at Week 1 (n=190, 186)	0.002 (± 0.345)	-0.044 (± 0.291)		
Change at Week 4 (n=184, 190)	0.051 (± 0.490)	-0.049 (± 0.000)		
Change at Week 8 (n=185, 187)	0.028 (± 0.463)	-0.039 (± 0.345)		
Change at Week 24 (n=150, 146)	0.051 (± 0.492)	-0.062 (± 0.403)		
Change at Week 36 (n=33, 34)	0.061 (± 0.273)	-0.053 (± 0.465)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Daily Oral Corticosteroid (OCS) Dose During Weeks 16-20 and Weeks 32-36

End point title	Percent Change from Baseline in Daily Oral Corticosteroid (OCS) Dose During Weeks 16-20 and Weeks 32-36

End point description:

Daily OCS dose is defined as total OCS dose in a day (accounting for reported dose and dose frequency) and converting the total daily dose to a prednisone-equivalent dose. Baseline dose is the prescribed OCS dose on the day of first dose of study drug in this study. Dose at Weeks 16-20 and 32-36 is the mean of all daily OCS doses during the week range. Percent change = 100 * (absolute change / baseline dose)

End point type	Secondary

End point timeframe:

Week 0 (baseline), Weeks 16-20, Weeks 32-36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: percent change				
arithmetic mean (standard deviation)				
% change at Week 16-20 (n=46, 45)	-2.19 (± 51.347)	-6.96 (± 40.904)		
% change at Week 32-36 (n=11, 11)	-8.44 (± 24.236)	-8.75 (± 29.666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Inhalations of Reliever Bronchodilator Medication: Baseline Values and Change from Baseline Values at Weeks 1, 4, 8, 24 and 36

End point title	Total Inhalations of Reliever Bronchodilator Medication: Baseline Values and Change from Baseline Values at Weeks 1, 4, 8, 24 and 36

End point description:

Total inhalations of reliever bronchodilator medication (eg, short-acting beta-agonist [SABA]) measured using weekly averages. The average was calculated as the sum of all values divided by the number of non-missing assessments. There was no imputation of missing data. At least 4 of the 7 measurements need to be recorded for a week to be included in the analysis; otherwise the week was treated as missing.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 1, 4, 8, 24, 36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: inhalations				
arithmetic mean (standard deviation)				
Baseline - observed values (n=171, 170)	2.4 (± 3.39)	2.6 (± 3.10)		
Change at Week 1 (n=158, 160)	-0.4 (± 1.30)	-0.4 (± 1.17)		
Change at Week 4 (n=153, 162)	-0.6 (± 1.86)	-0.5 (± 1.50)		
Change at Week 8 (n=155, 163)	-0.7 (± 1.79)	-0.6 (± 1.61)		
Change at Week 24 (n=121, 118)	-0.8 (± 1.92)	-0.8 (± 1.78)		
Change at Week 36 (n=23, 25)	-0.5 (± 1.69)	-0.6 (± 1.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Control Questionnaire-6 (ACQ-6) Total Score: Baseline Values and Change from Baseline Values at Weeks 8, 24 and 36

End point title	Asthma Control Questionnaire-6 (ACQ-6) Total Score: Baseline Values and Change from Baseline Values at Weeks 8, 24 and 36

End point description:

The ACQ-6 is a validated asthma assessment tool that has been widely used. There are 6 self-assessment questions. Each item on the ACQ-6 has a possible score ranging from 0 to 6 and the total score is the mean of all responses. The seven-point response scale: 0 = 'totally controlled' and 6 = 'severely uncontrolled.' Negative change from baseline values indicate improved asthma control.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 8, 24, 36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline - observed values (n=193, 195)	1.72 (± 1.098)	1.69 (± 1.171)		
Change at Week 8 (n=191, 192)	-0.31 (± 0.777)	-0.20 (± 0.718)		
Change at Week 24 (n=150, 145)	-0.30 (± 0.936)	-0.23 (± 0.771)		
Change at Week 36 (n=78, 77)	-0.34 (± 0.855)	-0.28 (± 0.867)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Quality of Life Questionnaire Administered to Participants Ages 12-70 years (AQLQ +12) Overall Score: Baseline Values and Change from Baseline Values at Weeks 8, 24 and 36

End point title	Asthma Quality of Life Questionnaire Administered to Participants Ages 12-70 years (AQLQ +12) Overall Score: Baseline Values and Change from Baseline Values at Weeks 8, 24 and 36

End point description:

The AQLQ +12 is a modified version of the standardized AQLQ, which was developed to measure functional impairments experienced by adults ≥17 years of age. The AQLQ +12 is valid for patients 12 to 70 years of age and includes 32 questions in 4 domains (symptoms, activity limitation, emotional function, and environmental stimuli). Participants were asked to recall their experiences during the previous 2 weeks and score each of the questions on a 7-point scale, where 7=not at all limited and 1=totally limited. The overall score of the AQLQ +12 was derived as the average of the 32 questions, thus, the total score ranges from 1 (indicates "total impairment") to 7 (indicates "no impairment"). Positive change from baseline values indicate improved quality of life.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Weeks 8, 24, 36

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	179		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline - observed value (n=186, 176)	5.04 (± 1.249)	5.14 (± 1.270)		
Change at Week 8 (n=185, 173)	0.30 (± 0.716)	0.14 (± 0.700)		
Change at Week 24 (n=143, 131)	0.28 (± 0.727)	0.20 (± 0.830)		
Change at Week 36 (n=72, 68)	0.32 (± 0.835)	0.19 (± 0.948)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Treatment-Emergent Anti-Drug Antibody (ADA) Responses

End point title	Participants with Treatment-Emergent Anti-Drug Antibody (ADA) Responses

End point description:

Treatment-emergent responses were defined as a positive sample post-baseline (negative baseline) OR a titer increase of >=4-fold relative to a positive baseline sample. Two types of antibody assay were performed, an immunogenicity status assay (ADA) and neutralizing assay (NAb). The ADA assay produces a positive or negative result. For samples with a positive result, a neutralizing assay was performed, which also produces a positive or negative result.

End point type	Secondary

End point timeframe:

Baseline - date of randomization in the previous study (C38072-AS-30025 or C38072-AS-30027), Weeks 8, 24, 36 or early withdrawal

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	196		
Units: participants	11	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Treatment-Emergent Anti-Drug Antibody (ADA) At the End-0f-Study Visit (Week 51)

End point title	Participants with Treatment-Emergent Anti-Drug Antibody (ADA) At the End-0f-Study Visit (Week 51)

End point description:

The endpoint was defined to evaluate immunogenicity after study drug washout since the end of study visit on Week 51 was to be 19 weeks after the final dose of study drug. Due to the early termination of the study no participants had an end of study visit.

End point type	Secondary

End point timeframe:

Week 51

End point values	Reslizumab 110 mg; Previous Treatment Placebo	Reslizumab 110 mg: Previous Treatment Reslizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: participants				

Notes:

[2] - Due to early termination, no participants had an end of study visit.

[3] - Due to early termination, no participants had an end of study visit.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to up to Day 269; for participants who discontinued early for reasons other than study termination, the timeframe was first dose of study drug to 4 weeks after the last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Reslizumab 110 mg

Reporting group description:

Participants were administered reslizumab 110 mg by subcutaneous injection every 4 weeks for a total of 9 doses.

Serious adverse events	Reslizumab 110 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 390 (4.10%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 390 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Synovial cyst			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonsillar abscess			
subjects affected / exposed	1 / 390 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 390 (0.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Reslizumab 110 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 390 (17.95%)		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	23 / 390 (5.90%)		
occurrences (all)	24		
Viral upper respiratory tract infection			
subjects affected / exposed	49 / 390 (12.56%)		
occurrences (all)	62		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported